# PEER REVIEW HISTORY

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## ARTICLE DETAILS

| TITLE (PROVISIONAL) | Optimising the quality of antibiotic prescribing in out-of-hours primary care in Belgium: a study protocol for an action research project |
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| AUTHORS | Colliers, Annelies; Coenen, Samuel; Philips, Hilde; Remmen, Roy; Anthierens, Sibyl |

## VERSION 1 - REVIEW

| REVIEWER | Sarah Tonkin-Crine<br>University of Oxford, UK<br>I have previously worked with two of the authors SC and SA on similar but unrelated projects. |
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| REVIEW RETURNED | 09-May-2017 |

| GENERAL COMMENTS | Introduction:<br>1. Last line of first paragraph, could also include additional Cochrane reviews, particularly those on point of care tests and shared decision making which are more recent that Arnold and Straus.<br>2. Citation needed at end of first sentence of second paragraph?<br>3. Paragraph 3 could make a better case for why the focus is on OOH. Presumably because previous work has been done 'in hours' and little is known about OOH care in Belgium? What potential does change in OOH have – how much does it contribute to abx prescribing overall?<br>4. Number of GPs in the GPC is not mentioned until very late on, would be useful to known earlier, when discussed in paragraph 3.<br>5. Last paragraph of the introduction is unclear in places and the first and last lines could be rephrased.<br><br>Methods<br>6. Would be useful to briefly list four typologies in action research.<br>7. Would be more information for a reader if the four year timeline was broken down into the three stages for clarity about how long each section will take.<br>8. Under Phase 1, could rephrase "strong and grounded interventions" for clarity.<br>9. Sentences on scientific rigour and coding of categories would be clearer with more detail (end of page 4).<br>10. Will data collected through videoing be analysed? Will it be shared with the clinician involved or the larger group? How many video consultations are likely to be discussed?<br>11. The reference to feedback on line 41 of page 6 indicates that the research team are anticipating some components of potential interventions. It would be useful to clarify, under phase 2, to what extent novel interventions are likely to be designed from scratch and/or how existing interventions are likely to be used and adjusted |

to the new OOH context.

12. Throughout the manuscript there is reference to intervention effectiveness and intervention implementation. It appears that the researchers are testing effectiveness rather than implementation (although the PAR methodology should help create something which can be implemented more easily). References to 'implementation strategies' could be described more clearly and the difference between strategies to support implementation and the actual interventions could be made explicit.

13. The research team appear to be targeting two behaviours of interest, unnecessary antibiotic prescribing and broad-spec prescribing. This could be acknowledged explicitly and authors could comment on whether this will require different interventions/intervention components.

14. It would be informative to know whether the research team plan to develop interventions aimed at the individual clinician, the clinician and any other relevant stakeholders and/or plan interventions at the GPC level as a whole.

15. Cite figure 1 in the main text where relevant.

16. It would be helpful for a reader to understand in more detail how the PAR approach will give information on transferability of findings to other contexts. Given that the approach involves co-design and a great deal of input from participants what does this mean for other areas of Belgium and other countries? How would other researchers determine whether findings are relevant to their context?

17. More information on how a theory or model would be constructed would be useful. Would this be purely based on the results of the study or also be informed by existing theory where relevant?

Discussion
18. Again the discussion could clarify how results of a PAR approach could inform interventions in other contexts (as mentioned above).

19. I would avoid references to "bad prescribers" as it indicates fault on behalf of clinicians. Prescribing not according to guidelines or prescribing which is not evidence-based may be more appropriate.

| REVIEWER | Robert Verheij<br>NIVEL (Netherlands Institute for Health Services Research), Netherlands |
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| REVIEW RETURNED | 25-May-2017 |

| GENERAL COMMENTS | Antibiotic prescribing in Belgium is still very problematic. This protocol describes a study that would help to reduce this problem. The concept of action research is appealing and fit for this purpose. However, I do have a number of questions:<br>1. Interventions/actions:<br>a. a problem with action research is that it is difficult to assess the effect of individual interventions on the outcome. How are the researchers going to deal with that?<br>b. How will the researchers keep track of all the interventions and who participates in them?<br>c. Who decides on what interventions will be organized, when and for whom?<br>2. Outcomes:<br>a. main outcome is the quality of prescribing in OOH services, which will be derived from electronic health records. A well known concern |
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with this type of data is data quality (eg [1 2]).How are researchers going to deal with that issue?

b. Outomes: How are patients involved in the study? I would think that also patients will have an opinion about a more restrictive antibiotic prescribing at the OOH. Is this also going to be measured? How?

c. to assess spill over, claims data from healthy insurance will be used. To what extent can this data be related to individual GP practices of doctors that also work at the OOH service?

3. Organisation

a. Is there a steering committee for the project: what organizations will be represented in it?

4. Privacy:

a. privacy issues. Regarding the video observations, informed consent from GPs is needed, but what about patients? Are they informed? And is this perhaps also one of the interventions (managing expectations of patients).

b. Privacy issues: is there a possibility that the Belgian implementation of the European General Data Protection Guideline will require informed consent from all patients also with respect to their electronic health record data?

c. Privacy issues: are patients informed of the use of 'their' data? How?

5. Minor comments:

a. P. 6, line 24: more valid than what?

b. P. 6, line 28: registration = recording

c. The authors may want to include references to the emerging literature on Learning Health Systems (eg [3] [4]).

References:

1. Barkhuysen P, de Grauw W, Akkermans R, et al. Is the quality of data in an electronic medical record sufficient for assessing the quality of primary care? Journal of the American Medical Informatics Association 2014;21(4):692-98 doi: 10.1136/amiajnl-2012-001479[published Online First: Epub Date]|.

2. van der Bij S, Khan N, Ten Veen P, et al. Improving the quality of EHR recording in primary care: a data quality feedback tool. Journal of the American Medical Informatics Association : JAMIA 2016 doi: 10.1093/jamia/ocw054[published Online First: Epub Date]|.

3. Friedman C, Rubin J, Brown J, et al. Toward a science of learning systems: a research agenda for the high-functioning Learning Health System. Journal of the American Medical Informatics Association : JAMIA 2015;22(1):43-50 doi: 10.1136/amiajnl-2014-002977[published Online First: Epub Date]|.

4. Delaney BC, Peterson KA, Speedie S, et al. Envisioning a learning health care system: the electronic primary care research network, a case study. Annals of family medicine 2012;10(1):54-9 doi: 10.1370/afm.1313[published Online First: Epub Date]|.

Reviewer 1:

Introduction:
1. Last line of first paragraph, could also include additional Cochrane reviews, particularly those on point of care tests and shared decision making which are more recent that Arnold and Straus.

Thank you for this comment. The two mentioned articles are indeed very relevant and were added to the reference list.

-Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database Syst Rev 2005(4):CD003539.
-Aabenhus R, Jensen JUS, Jorgensen KJ, et al. Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. Cochrane Db Syst Rev 2014(11): CD010130.
-Coxeter P, Del Mar CB, McGregor L, Beller EM, Hoffmann TC. Interventions to facilitate shared decision making to address antibiotic use for acute respiratory infections in primary care. Cochrane Database Syst Rev. 2015(11):CD010907.

2. Citation needed at end of first sentence of second paragraph?

Indeed a citation is needed. We have provided a link to the Belgian guide to treatment of infections in ambulatory care (www.pubmed.be/832250_BW_NL_01_84_IC.pdf) and a link to the website of the editor of this guide, i.e. the Belgian Antibiotic Policy Coordination Committee (BAPCOC; http://consultativebodies.health.belgium.be/en/advisory-and-consultative-bodies/commissions/BAPCOC). BAPCOC is part of the Belgian federal public service health, food chain safety and environment, aiming to promote rational antibiotic consumption in Belgium and involved in organising interventions for the public and professionals.

3. Paragraph 3 could make a better case for why the focus is on OOH. Presumably because previous work has been done 'in hours' and little is known about OOH care in Belgium? What potential does change in OOH have – how much does it contribute to ab prescribing overall?

Indeed the main focus of research on antibiotic prescribing in primary care so far has been rather on 'during office hours' than on OOH care (in Belgium). Research in the OOH setting potentially offers us many opportunities to improve antibiotic prescribing since it provides us with access to reach a large and diverse group of GPs, who are more difficult to reach in their own private practices during office hours, and any improvements in this setting could have a spill over effect in their individual day to day practices.
At this point we don't have detailed insights into the quantity and quality differences in antibiotic prescribing globally in Belgium during office and outside office hours, except what N. Adriaenssens et al. described for one specific GPC: "Adriaenssens N et al. Quality of antibiotic prescription during office hours and out-of-hours Flemish primary care, using European quality indicators. Eur J Gen Pract 2014;20:114-20." Dutch and Danish research teams found equal and even better quality of prescribing in OOH-care than during office hours, but both already are low-prescribing countries.

Following sentence was added to the paragraph to clarify:

"Until now detailed data on the quantity and quality of antibiotic prescribing in OOH care in Belgium, like research on antibiotic prescribing in OOH care in Belgium is scarce. Research showed high antibiotic prescribing in OOH care in Denmark, while in the Netherlands it showed slightly better prescribing quality than during office hours. Both are low prescribing countries. In the described project, interventions will be targeted at 170 GPs of one GPC. But antibiotic prescribing data of three neighbouring GPCs will be available as well to get a more detailed insight in GPs' prescribing habits in Belgian OOH care."

Ref.:
-Debets VE, Verheij TJ, van der Velden AW, et al. Antibiotic prescribing during office hours and out-of-hours: a comparison of quality and quantity in primary care in the Netherlands. Br J Gen Pract 2017;67(656):e178-e86.
-Huibers L, Moth G, Christensen MB, et al. Antibiotic prescribing patterns in out-of-hours primary care: a population-based descriptive study. Scand J Prim Health Care 2014;32(4):200-7.

4. Number of GPs in the GPC is not mentioned until very late on, would be useful to known earlier, when discussed in paragraph 3.

The following sentence was added to clarify earlier on in the article the number of GPs that are involved in the GPC setting in paragraph 3.

"In the described project, interventions will be targeted at 170 GPs of one GPC."

5. Last paragraph of the introduction is unclear in places and the first and last lines could be rephrased.

Thank you for this comment. We have rephrased the following sentences to improve the paragraph. The last paragraph was rephrased as followed:

"Therefore, in this study we will use the PAR approach to improve the quality of antibiotic prescribing for acute infections in primary care. The goal is to co-create and set up interventions together with the GPs of a GPC. As outcomes we will use APQI and antibiotic use data to assess a possible spill over effect from the intervention in OOH care to office hours. In addition, we will assess the feasibility and acceptability of PAR in this setting. And we will describe what can be learned from its success factors and barriers."

Methods
6. Would be useful to briefly list four typologies in action research.

Thank you for this suggestion. The following sentence was added:

"Those four types are the experimental, organizational, professionalizing and empowering type of action research."

7. Would be more information for a reader if the four year timeline was broken down into the three stages for clarity about how long each section will take.

Thank you for this suggestion. The following sentence was added to clarify how long each section will take:
"In the first year, we plan to complete the first exploring phase, in the second and third year the facilitating change phase and in the last year we plan to run a detailed evaluation of the project."

8. Under Phase 1, could rephrase "strong and grounded interventions" for clarity.

We rephrased the sentence as follows:

"By better understanding GPs' behaviour and taking into account the different barriers they experience, we will be able to understand their conduct and to develop interventions with better chances of success and bigger support from the GPs."

9. Sentences on scientific rigour and coding of categories would be clearer with more detail (end of page 4).

Thank you for this suggestion. The following sentence was added:

"The GPs who have contributed to the interviews will receive a formal analysis report with the summary of the findings and will be asked to deliver feedback (member checking, but also reflecting on it) in a focus group. And in a second phase this will be made available to all GPs of the GPC. Coding of the first three to five interviews will be done by two researchers independently (AC, a GP and SA, a sociologist). The coding framework will then be developed by consensus of these two researchers. Following the independent coding, the initial thematic framework will be compared, and similarities and differences will be discussed and amended to create a set of themes that represents both analyses. This thematic framework will be used for further analysis and if new themes emerge this will be discussed amongst the research team. The interim analyses will be critically looked at by the other three members of the multidisciplinary research team and will be adapted after their feedback."

10. Will data collected through videoing be analysed? Will it be shared with the clinician involved or the larger group? How many video consultations are likely to be discussed?

Thank you for these questions. To clarify this part of the study, the following sentence was added explaining how the video material is intended to be used:

"The data collected through video observations will be analysed on the one hand for research purposes and on the other hand to guide the intervention development. During the interviews of phase 1 the use of video-observations and possible related barriers will be discussed with the participants. During the interviews we explore the thoughts of the GPs about receiving personal feedback or the possibility to discuss the videos with one of the researchers or with their peers. Another question is asked about the thoughts about using the videos solely as transcripts for research or also for peer education, or even to use them in video-format with peers. Hence, the way we will use the video material will depend on the willingness or preference of the participants in our action research."

11. The reference to feedback on line 41 of page 6 indicates that the research team are anticipating some components of potential interventions. It would be useful to clarify, under phase 2, to what extent novel interventions are likely to be designed from scratch and/or how existing interventions are likely to be used and adjusted to the new OOH context.

The PAR approach is based on the equality between researchers and participants and we plan to conform to this philosophy by engaging the GPs to come up with their own solutions in discussion with the research team.

The research team consists of people with a lot of knowledge on OOH care and experience with antibiotic improvement strategies so they will support the GPs in making a grounded decision. The

example of the GRACE INTRO was added to clarify the idea behind process indicators. Following sentence was added to clarify this:

"At this point the research group does not have a preference for the type of interventions that will be implemented, but they do have the knowledge of existing, appropriate and effective interventions to support the GPs' wishes and needs."

12. Throughout the manuscript there is reference to intervention effectiveness and intervention implementation. It appears that the researchers are testing effectiveness rather than implementation (although the PAR methodology should help create something which can be implemented more easily). References to 'implementation strategies' could be described more clearly and the difference between strategies to support implementation and the actual interventions could be made explicit.

Thank you for this suggestion. We are indeed looking at both effectiveness and implementation strategies.

"Participatory Action Research refers to a range of research methods that emphasise participants and action (that is implementation) using methods that involve iterative processes of reflection and action. Although most of the PAR methods involve qualitative techniques, increasingly quantitative and mixed methods are used, which we will also combine. The main emphasis however is on the process. The main objectives are to explore, to see whether the process is adequate (to see whether the intervention and outcomes are occurring (so is there a change in prescribing) and to explain (how and why does implementation of the intervention lead to effects, so develop or expand a theory to explain the relationships between concepts and the reason for the change)."

And:

"There are recognised difficulties in measuring effectiveness of interventions in PAR and using PDSA cycles, because of the many variables in a complex situation. The evaluation of action research therefore is not solely a change intervention, but more a research approach with change and knowledge outcomes, where qualitative findings on context, process and views of participants are a part of."

Ref.:
-Peters DH, Adam T, Alonge O, et al. Implementation research: what it is and how to do it. Bmj-Brit Med J 2013;347.
-Peters DH, Tran N, Adam T. Implementation research in health: a practical guide. Alliance for Health Policy and Systems Research, World Health Organization 2013.
-Reason P, Bradbury H. The SAGE Handbook of Action Research: Participative Inquiry and Practice. Sage Publications Ltd 2008;2nd edition.
-Reed JE, Card AJ. The problem with Plan-Do-Study-Act cycles. BMJ Qual Saf 2016;25(3):147-52.

13. The research team appear to be targeting two behaviours of interest, unnecessary antibiotic prescribing and broad-spec prescribing. This could be acknowledged explicitly and authors could comment on whether this will require different interventions/intervention components.

Thank you for this suggestion. Our focus is indeed on both unnecessary antibiotic prescribing and broad-spec prescribing. But it can be that the GPs involved would like to focus on one specific problem.

This was clarified as follows:

"In the data-analyses, the focus will be on lowering antibiotic prescribing as well as on improving the proportion of receiving a recommended antibiotic and lowering the use of broad-spectrum antibiotics. But, the involved GPs can choose to develop interventions that target all these elements or target only one specific problem. The participants will have their saying not only in the action process itself, but also on how it will be evaluated so matching interventions and assessments have to be chosen."

14. It would be informative to know whether the research team plan to develop interventions aimed at the individual clinician, the clinician and any other relevant stakeholders and/or plan interventions at the GPC level as a whole.

Thank you for this suggestion. The plan is to develop interventions that focus on the GPC as a whole and the relevant stakeholders: the individual GPs, the patients and other relevant stakeholders that might be elicited during the interviews in phase 1. The intervention (s) will be co-created with the stakeholders and therefore at this stage it is unclear how the intervention will look like. However, it will be individual GP on call who will undergo the intervention.

Following sentence was added:

"Interventions will be delivered and assessed at GPC level, but since the intervention(s) will be co-created with the stakeholders, at this stage it is unclear how the intervention will be look like and who it will be aimed at, the individual GP, the patients, both or any other relevant stakeholder or structure. Every GP of the region is on call for several times every year and will thus be exposed to the intervention(s)."

15. Cite figure 1 in the main text where relevant.

Figure 1 was cited in the second paragraph of the methods section.

16. It would be helpful for a reader to understand in more detail how the PAR approach will give information on transferability of findings to other contexts. Given that the approach involves co-design and a great deal of input from participants what does this mean for other areas of Belgium and other countries? How would other researchers determine whether findings are relevant to their context?

The question about transferability arises often when action research is used. We added following paragraph to the discussion section:

"Findings of every phase of the research will be discussed and published within the PAR approach and will be provided with rich contextual details to judge relevance for the reader's own context. Generalisation of action research is not empirically based, but theoretically constructed. The idea is not to seek generalizable data, but generate knowledge. Critical reflection within the research group and with the stakeholders will continuously feed this knowledge and will sketch the research within a certain context."

17. More information on how a theory or model would be constructed would be useful. Would this be purely based on the results of the study or also be informed by existing theory where relevant?

Thank you for this suggestion. The following sentence was added:

"The main objectives are to explore, to see whether the process is adequate (to see whether the intervention and outcomes are occurring (so is there a change in prescribing)) and to explain (how and why does implementation of the intervention lead to effects, (so develop or expand a theory to

explain the relationships between concepts and the reason for the change)."

Discussion
18. Again the discussion could clarify how results of a PAR approach could inform interventions in other contexts (as mentioned above).

We hope to have answered this suggestions before (See point 16).

19. I would avoid references to "bad prescribers" as it indicates fault on behalf of clinicians. Prescribing not according to guidelines or prescribing which is not evidence-based may be more appropriate.

Indeed a very relevant remark. We adapted the phrase to:

"Antibiotic rates vary between different GPs. The impact of this intervention on GPs can differ between the prescribers who are adhering to guidelines or the ones that are not. Attention should be paid on involving and motivating these last ones."

Reviewer 2:
1. Interventions/actions:
a. a problem with action research is that it is difficult to assess the effect of individual interventions on the outcome. How are the researchers going to deal with that?

Thank you for this question. This is indeed a challenge. We will try to work with well-defined interventions and if necessary implement these one by one, evaluation them through PDSA cycles. Interventions will be at GPC level. Every GP of the region is on call for several times every year and will thus be exposed to the intervention(s).

Following sentences were added:

"Interventions will be delivered and assessed at GPC level, but since the intervention (s) will be co-created with the stakeholders, at this stage it is unclear how the intervention will be look like and who it will be aimed at, the individual GP, the patients, both or any other relevant stakeholder or structure. Every GP of the region is on call for several times every year and will thus be exposed to the intervention(s). There are recognised difficulties in measuring effectiveness of interventions in PAR and using PDSA cycles, because of the many variables in a complex situation. The evaluation of action research therefore is not solely a change intervention, but more a research approach with change and knowledge outcomes, where qualitative findings on context, process and views of participants are a part of."

And

"Participatory Action Research refers to a range of research methods that emphasise participants and action (that is implementation) using methods that involve iterative processes of reflection and action. Although most of the PAR methods involve qualitative techniques, increasingly quantitative and mixed methods are used, which we will also combine.

The main emphasis however is on the process. The main objectives are to explore, to see whether the process is adequate (to see whether the intervention and outcomes are occurring (so is there a change in prescribing)) and to explain (how and why does implementation of the intervention lead to effects, (so develop or expand a theory to explain the relationships between concepts and the reason

for the change)."

Ref.:
-Reason P, Bradbury H. The SAGE Handbook of Action Research: Participative Inquiry and Practice. Sage Publications Ltd 2008;2nd edition.
-Reed JE, Card AJ. The problem with Plan-Do-Study-Act cycles. BMJ Qual Saf 2016;25(3):147-52.
-Peters DH, Adam T, Alonge O, et al. Implementation research: what it is and how to do it. Bmj-Brit Med J 2013;347.
-Peters DH, Tran N, Adam T. Implementation research in health: a practical guide. Alliance for Health Policy and Systems Research, World Health Organization 2013.

b. How will the researchers keep track of all the interventions and who participates in them?

Thank you for this question. We will keep track of all the interventions and evaluate them closely. Interventions will be well-defined and if necessary implemented one by one and evaluated through PDSA cycles. The indicators to measure the process and outcome will be set up together with the stakeholders.

Following sentence was added:

"Interventions will be delivered and assessed at GPC level, but since the intervention (s) will be co-created with the stakeholders, at this stage it is unclear how the intervention will be look like and who it will be aimed at, the individual GP, the patients, both or any other relevant stakeholder or structure. Every GP of the region is on call for several times every year and will thus be exposed to the intervention(s). There are recognised difficulties in measuring effectiveness of interventions in PAR and using PDSA cycles, because of the many variables in a complex situation. The evaluation of action research therefore is not solely a change intervention, but more a research approach with change and knowledge outcomes, where qualitative findings on context, process and views of participants are a part of."

c. Who decides on what interventions will be organized, when and for whom?

Thank you for your question.
We have tried to clarify this issue by adding following phrases in the method section.

"At this point the research group does not have a preference for the type of interventions that will be implemented, but they do have the knowledge of existing, appropriate and effective interventions to support the GPs wishes and needs. The intervention will be co-created with the stakeholders."

And:

"Interventions will be delivered and assessed at GPC level, but since the intervention (s) will be co-created with the stakeholders, at this stage it is unclear how the intervention will be look like and who it will be aimed at, the individual GP, the patients, both or any other relevant stakeholder or structure. Every GP of the region is on call for several times every year and will thus be exposed to the intervention(s).

2. Outcomes:
a. main outcome is the quality of prescribing in OOH services, which will be derived from electronic health records. A well known concern with this type of data is data quality (eg [1 2]).How are researchers going to deal with that issue?

Data quality is indeed one of our concerns. Within the iCAREdata project one of the key goals is to ensure the quality of data registration by all health care providers. Belgian GPCs work with a high-quality, encoded, electronic registration of patient contacts, i.e. reasons for encounter, clinical diagnosis, and prescriptions. These registrations are obligatory. Within iCAREdata a quality manager is appointed, whose task is to perform the quality control and feedback of the incoming data. We described these specifics in the following paper: "Colliers A, Bartholomeeusen S, Remmen R, et al. Improving Care And Research Electronic Data Trust Antwerp (iCAREdata): a research database of linked data on out-of-hours primary care. BMC Res Notes 2016;9:259." (ref 32) Data of other surrounding GPCs can serve as a control group to follow-up our data through time.

The following phrases are already in the manuscript:

"GPs are required to record diagnosis and treatment in an electronic medical health record. But the quality of these quantitative data depends on the GPs who record their patient contacts and could be a limitation."

We added the following sentences to the discussion section:

"In this project the quality of the data depends on the quality of recording by the GPs in their electronic health record at the GPC. We will monitor the quality of these data closely and critically reflect on the relevance for clinical practice."

b. Outcomes: How are patients involved in the study? I would think that also patients will have an opinion about a more restrictive antibiotic prescribing at the OOH. Is this also going to be measured? How?

Thank you for these questions. The feasibility and acceptability of the implemented interventions will be studied from the perspectives of the GPs, but also from the perspective of the patients. This means that in the "study phase" of the PDSA cycle there will not only be an evaluation of the quantitative prescribing data, but also on the thoughts of GPs and possibly patients. Depending on the type of intervention(s) that will be implemented patients' ideas will be questioned for example through a short questionnaire or a telephone interview.

The following paragraph with an example is already in the manuscript:

"The feasibility and acceptability of the implemented interventions will be studied from the perspectives of the GPs, but also from the perspective of the patients. Process indicators will depend on the type of interventions and implementation strategies chosen by the stakeholders. If, for example, they choose for an internet-based communication skills training such as GRACE INTRO, the number of patient information booklets, which are an integral part of this intervention, distributed to patients could serve as a process indicator. But also the experiences, views, acceptability, etc. of patients receiving this intervention will be explored and be taken into account into the adaptation of the interventions."

And the following sentence was added:

"Interventions will be delivered and assessed at GPC level, but since the intervention (s) will be co-created with the stakeholders, at this stage it is unclear how the intervention will be look like and who it will be aimed at, the individual GP, the patients, both or any other relevant stakeholder or structure. Every GP of the region is on call for several times every year and will thus be exposed to the

intervention(s).

c. to assess spill over, claims data from healthy insurance will be used. To what extent can this data be related to individual GP practices of doctors that also work at the OOH service?

Thank you for this question. In Belgium every GP is obliged to be on call in the GPC of his/her own region. Individual linking of data within and in OOH care is not possible.

The following sentences were added:
"In Belgium every GP is obliged to be on call in the GPC of his/her own region, meaning that one GPC covers all the GPs of one specific well-defined region."

And:

"Interventions will be delivered and assessed at GPC level, but since the intervention (s) will be co-created with the stakeholders, at this stage it is unclear how the intervention will be look like and who it will be aimed at, the individual GP, the patients, both or any other relevant stakeholder or structure. Every GP of the region is on call for several times every year and will thus be exposed to the intervention(s)."

3. Organisation
a. Is there a steering committee for the project: what organizations will be represented in it?

Thank you for this question.

The 5 involved researchers have a formal meeting every month to follow up the project that is part of a PhD thesis. There are regular updates and contacts with the board of the GPC.
iCAREdata has a scientific advisory board composed of representatives from the university department and all partners involved in the project, i.e. representatives of the four GPCs of Antwerp. The scientific advisory board evaluates the research requests for iCAREdata use.

4. Privacy:
a. privacy issues. Regarding the video observations, informed consent from GPs is needed, but what about patients? Are they informed? And is this perhaps also one of the interventions (managing expectations of patients).

Thank you for these questions. For the video observation study a new ethical approval will be applied for including the privacy issues of the patients and the GPs, as mentioned in the protocol ("As each WP of the study develops, amendments might be applied for.") This will include an information leaflet and informed consent. We have recently questioned patients through a structured questionnaire about their thoughts and ideas on video observations during consultations in OOH care to guide the setup of this work package.

b. Privacy issues: is there a possibility that the Belgian implementation of the European General Data Protection Guideline will require informed consent from all patients also with respect to their electronic health record data?
c. Privacy issues: are patients informed of the use of 'their' data? How?

The implementation of the European General Data Protection Guideline will not change anything in the consent procedure of the use of the database, due to the already strict Belgian privacy laws. As for as the use of the quantitative data to evaluate antibiotic prescribing, the privacy issues are described within the iCAREdata project. iCAREdata is funded by the FWO and managed by the

Department of Primary and Interdisciplinary Care (Centre for General Practice) of the University of Antwerp.

"Ethics approval for data extraction from the electronic medical records for all GPCs in iCAREdata was granted by the Ethics Committee of the University of Antwerp/University Hospital Antwerp (12/49/404 and 13/34/330).
To secure the privacy of information about individual patients, a permission for the data collection at the GPCs was obtained from the Committee of Health of the Commission for the Protection of Privacy (N° 14/094 n173 on November 18th, 2014). A separate application for the data-linkage was approved on July 28th, 2015 (N° 14/194 n133).
An official request to use these specific antibiotic data will be made to the scientific advisory board of iCAREdata. Patients are informed through a poster and leaflets in the waiting room and there is an opt-out system in place."
This information was added to the ethics section.

5. Minor comments:
a. P. 6, line 24: more valid than what?

Thank you for this comment. To clarify this the following sentence was added:

"Hence, the latter outcome measurement will have complete response, and will not interfere with the normal routine of the eligible GPs, allowing a more valid estimate of any spill over effect than databases who recover data from the recording by GPs into their own system."

b. P. 6, line 28: registration = recording

Thank you for this comment. We changed the word 'registration' into 'recording'. We adapted the rephrasing throughout the manuscript.

"The quality of the IMA data does not depend on the quality of recording by the GPs, in contrast to the OOH care data."

c. The authors may want to include references to the emerging literature on Learning Health Systems (eg [3] [4]).

Thank you for this suggestion. A paragraph in the discussion section was added to focus on this subject with the relevant references.

"The use of routinely collected data for research purposes and to improve care is gaining more and more interest under the term "Learning Healthcare systems". It offers tremendous possibilities to improve clinical practice. But is also poses challenges such as data quality, security issues, technical support, etc. In this project the quality of the data depends on the quality of recording by the GPs in their electronic health record at the GPC. We will monitor the quality of these data closely and critically reflect on the relevance for clinical practice."


Ref:
-Delaney BC, Peterson KA, Speedie S, et al. Envisioning a learning health care system: the electronic primary care research network, a case study. Ann Fam Med 2012;10(1):54-9.
-Friedman C, Rubin J, Brown J, et al. Toward a science of learning systems: a research agenda for the high-functioning Learning Health System. J Am Med Inform Assoc 2015;22(1):43-50.
-Delaney BC, Curcin V, Andreasson A, et al. Translational Medicine and Patient Safety in Europe:

TRANSFoRm--Architecture for the Learning Health System in Europe. Biomed Res Int 2015;2015:961526.
-Barkhuysen P, de Grauw W, Akkernnans R, et al. Is the quality of data in an electronic medical record sufficient for assessing the quality of primary care? J Am Med Inform Assn 2014;21(4):692-98.
-van der Bij S, Khan N, Ten Veen P, et al. Improving the quality of EHR recording in primary care: a data quality feedback tool. J Am Med Inform Assoc 2017;24(1):81-87

**VERSION 2 – REVIEW**

| REVIEWER | Sarah Tonkin-Crine<br>University of Oxford, UK<br>I have previously published research with two of the authors of this manuscript. |
|---|---|
| REVIEW RETURNED | 27-Jun-2017 |

| GENERAL COMMENTS | I have a couple of very minor comments which are only suggestions for improvements:<br><br>1. Last paragraph of introduction reads like the only outcome will be assessing the spill over effect in "in hours" practice. Authors could rephrase this sentence. In addition the last sentence of this paragraph ending "factors and barriers" is unclear.<br><br>2. Under "Phase 3" a sentence states "The concept of analytic generalisation allows to apply the research findings not only in similar contexts, but to other groups and contexts as well". This is still difficult for a reader to understand and could be clarified. In the discussion the authors also state that "the idea is not to seek generalizable data, but generate knowledge". This also could be clarified.<br><br>3. There are minor grammatical errors throughout the new sections of text. |
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| REVIEWER | Robert Verheij<br>NIVEL, Netherlands Institute for Health Services Research |
|---|---|
| REVIEW RETURNED | 30-Jun-2017 |

| GENERAL COMMENTS | Comments of both reviewers have been processed in an adequate way. |
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**VERSION 2 – AUTHOR RESPONSE**

We have made following changes to the text to meet the editorial requirements:
- We revised the title of the manuscript:
"Optimising the quality of antibiotic prescribing in out-of-hours primary care in Belgium: a study protocol for an action research project"
- The conclusion section was removed. The text was integrated in the discussion section.
- The bulletpoints were shortened to one sentence each.

We believe we have addressed all the reviewer's comments.

1.The last paragraph of the introduction was changed to:

"The goal is to co-create and set up interventions together with the GPs of a GPC. As outcomes we will use APQI to assess the quality of antibiotic prescribing at the GPC and antibiotic use data to assess a possible spill over effect from the intervention in OOH care to office hours. In addition, we will assess the feasibility and acceptability of PAR in this setting. And we will describe what can be learned from the success factors and barriers of using the PAR approach to improve antibiotic prescribing in OOH primary care."

2.To clarify the sentences under "phase 3" and the discussion" section following changes were made:

"The concept of analytic generalisation, by linking our particular findings to theory, allows to apply the research findings not only in similar contexts, but to other groups and contexts as well."

"Generalisation of action research is not empirically based, but theoretically constructed. 55 Our findings will only be generalisable within our own specific context and situation. The idea is not to seek generalizable data, but generate knowledge."

3. Troughout the text small changes were made to improve readibility and to correct grammatical errors.